Remarks

Claims 1 and 7 to 10 have been amended. Claim 2 has been cancelled without prejudice or disclaimer and with the understanding that the cancelled subject matter may be pursued in a continuation application. The amendments to claims 1, 9 and 10 incorporate the features of claim 2, now cancelled. The amendment to claim 7 reflects the cancellation of claim 2, from which claim 7 depended. The amendment to claim 8 identifies obesity and/or diabetes as specific diseases/conditions mediated through glucokinase. Support for this amendment may be found in the specification at, *inter alia*, page 2, lines 15-30, page 10, lines 24-26 and page 11, lines 7-13. No new matter has been introduced by any of the amendments.

Based on the Examiner's comments in the present office action (*e.g.*, that claims 9 and 10 depend from rejected base claims – see the "Claim Objections" section), it appears that the Examiner did not consider the preliminary amendment that was filed with the subject application on May 12, 2005. In the preliminary amendment, for example, claims 9 and 10 were rewritten as independent claims. Although a copy of the preliminary amendment exists in the image file wrapper of the subject application on the PAIR website of the U.S. Patent Office, Applicants submit for the Examiner's convenience a copy of the preliminary amendment herewith. The amendments to the claims in the presently filed Amendment and Response are based on the claims as amended in the preliminary amendment.

1. **Rejection under 35 U.S.C. § 112, first paragraph**

Claim 8 is rejected by the Examiner as failing to comply with the written description requirement because the Examiner asserts that Applicants' specification allegedly does not adequately describe the nexus between the mediation through glucokinase and a useful treatment of a disease/condition. Further, the Examiner rejects claim 8 as also failing to comply with the enablement requirement, presenting as support for this rejection a brief *In re Wands* analysis of claim 8.

Applicants respectfully disagree with the Examiner's rejections of claim 8, but in order to expedite prosecution of the subject application, have amended claim 8 to delete the "mediated

through glucokinase" language that appears to form the basis for the Examiner's rejections. Accordingly, Applicants respectfully request that the rejections be withdrawn.

2. Rejections under 35 U.S.C. § 102(a)

Claims 1, 5, 7 and 8 are rejected as allegedly being anticipated by WO 02/24682 too Angibaud. The Examiner specifically cites a compound with the registry number 405549-65-7.

Applicants have, in order to expedite prosecution of the subject application, amended claims 1, 9 and 10 such that the other of R^1 and R^2 is C_{1-4}alkoxy. In light of this amendment, Applicants respectfully request that this rejection by the Examiner be withdrawn.

3. Claim Objections

Claims 2 to 4, 6, 9 and 10 are objected to because the Examiner asserts that they depend from rejected base claims.

Applicants believe that in light of the amendments to claims 1, 9 and 10, claims 2 to 4, 6, 9 and 10 should be in a condition for allowance.

4. Conclusion

Upon consideration of the foregoing, it will be recognized that Applicants have fully and appropriately responded to all of the Examiner's rejections. Accordingly, all claims are believed to be in proper form in all respects and a favorable action on the merits is respectfully requested. Should the Examiner feel that there are any issues outstanding after consideration of this response, the Examiner is invited to contact Applicants' undersigned representative to expedite prosecution.

Except for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or to credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **constructive petition for extension of time** in accordance with 37 C.F.R. 1.136(a)(3).

Morgan, Lewis & Bockius LLP

Gregory T. Lowen
Registration No. 46,882
Direct: 202-739-5915

Date: June 30, 2006

CUSTOMER NO. 009629
Morgan, Lewis & Bockius LLP
1111 Pennsylvania Ave., N.W.
Washington, D.C. 20004
Tel.: 202-739-3000
Fax: 202-739-3001

Docket No.: ASZD-P01-898
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Hargreaves et al.

Application No.: Not Yet Assigned

Confirmation No.: Not Yet Assigned

Filed: May 12, 2005

Art Unit: Not Yet Assigned

For: QUINOLINE DERIVATIVES AS GLUCOKINASE LIGANDS

Examiner: Not Yet Assigned

FIRST PRELIMINARY AMENDMENT

MS PCT
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

COPY

Dear Sir:

INTRODUCTORY COMMENTS

Prior to examination on the merits, please amend the above-identified U.S. patent application as follows:

Amendments to the Specification begin on page 2 of this paper.

Amendments to the Claims are reflected in the listing of claims which begins on page 3 of this paper.

Remarks/Arguments begin on page 9 of this paper.

Amendments to the Specification:

On Page 1, please insert the following paragraph immediately after the title:

Related Applications

This application is a national stage filing under 35 U.S.C. 371 of International Application PCT/GB2003/004915, filed November 13, 2003, which claims priority from United Kingdom Application No. 0226931.4, filed November 19, 2002, the specifications of each of which are incorporated by reference herein. International Application PCT/GB2003/004915 was published under PCT Article 21(2) in English.

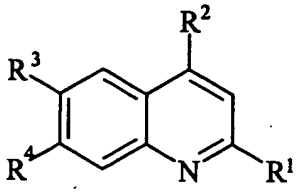
Please insert the Abstract, appearing on a separate page herewith, immediately after the last page of the claims.

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims

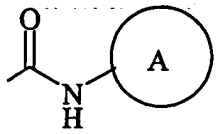
1. (Currently Amended) A compound of formula (I):



(I)

wherein:

~~One~~ one of R^1 and R^2 is ~~selected from~~ a group (IA):



(IA)

and the other R^1 or R^2 is selected from hydrogen, C_{1-4}alkyl, C_{1-4}alkoxy, carbocyclyl, heterocyclyl, carbocyclyloxy and heterocyclyloxy; wherein this R^1 or R^2 ~~may be~~ is optionally substituted on carbon by one or more groups selected from R^5; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen ~~may be~~ is optionally substituted by C_{1-4}alkyl;

Ring A is pyridin-2-yl or thiazol-2-yl; wherein said pyridin-2-yl or thiazol-2-yl ~~may be~~ is optionally substituted on carbon by one or more groups selected from R^6;

one of R^3 and R^4 is hydrogen and the other is selected from hydrogen, C_{1-4}alkyl, C_{1-4}alkoxy, carbocyclyl, heterocyclyl, carbocyclyloxy and heterocyclyloxy; wherein R^3 and R^4 ~~may be~~ are independently optionally substituted on carbon by one or more groups selected from R^7; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen ~~may be~~ is optionally substituted by C_{1-4}alkyl;

R^6 is selected from halo, carboxy and C_{1-4}alkyl;

R^5 and R^7 are independently selected from halo, C_{1-4}alkyl, C_{1-4}alkoxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, carbocyclyl, heterocyclyl, carbocyclyloxy, heterocyclyloxy and carbocyclylidenyl; wherein R^5 and R^7 ~~may be~~ is independently optionally substituted on carbon by one or more R^8; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen ~~may be~~ is optionally substituted by C_{1-4}alkyl; and

R^8 is selected from halo, carboxy, methyl, ethyl, methoxy, ethoxy, methylamino, ethylamino, dimethylamino, diethylamino and *N*-methyl-*N*-ethylamino;

or a salt, solvate or pro-drug thereof.

2. (Currently Amended) A compound according to Claim 1 wherein one of R^1 and R^2 is selected from a group **(IA)** and the other of R^1 ~~or~~ and R^2 is selected from C_{1-4}alkoxy; wherein this R^1 or R^2 ~~may be~~ is optionally substituted on carbon by one or more groups selected from R^5.

3. (Currently Amended) A ~~compounds~~ compound according to Claim 2 wherein Ring **A** in the group **(IA)** is substituted by carboxy and the C_{1-4}alkoxy group is substituted on carbon by one or more groups selected from R^5.

4. (Original) A compound according to Claim 3 wherein R^5 is selected from carbocyclyl optionally substituted by one or more R^8.

5. (Currently Amended) A compound according to ~~any one of the preceding claims~~ Claim 1 wherein one of R^3 and R^4 is hydrogen and the other is C_{1-4}alkyl.

6. (Original) A compound according to Claim 1 selected from:

2-(2-Chlorobenzyloxy)-4-[*N*-(5-carboxythiazol-2-yl)carbamoyl]-6-methylquinoline;

2-(2-Chlorobenzyloxy)-4-[*N*-(5-carboxythiazol-2-yl)carbamoyl]-quinoline;

2-(2-Chlorobenzyloxy)-4-[*N*-(5-carboxypyrid-2-yl)carbamoyl]-6-methylquinoline;

2-(2-Chlorobenzyloxy)-4-[*N*-(5-carboxypyrid-2-yl)carbamoyl]-quinoline;

2-[*N*-(5-carboxypyrid-2-yl)carbamoyl]-4-(2-methylbenzyloxy)-quinoline; and

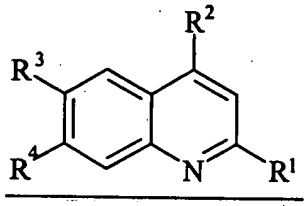
2-(1-methylpropoxy)-4-[*N*-(5-carboxythiazol-2-yl)carbamoyl]-quinoline;

or a salt, solvate or pro-drug thereof.

7. (Original) A pharmaceutical composition comprising a compound according to any one of Claims 1 to 6, or a salt, pro-drug or solvate thereof, together with a pharmaceutically acceptable diluent or carrier.

8. (Currently Amended) A method of treating a disease mediated through glucokinase, comprising administering a compound according to any one of Claims 1 to ~~6 for use in the preparation of a medicament for treatment of a disease mediated through GLK~~.

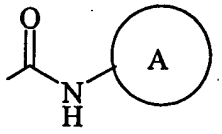
9. (Currently Amended) A process for preparing a compound ~~according to Claim 1~~ of formula (I):



(I)

wherein:

one of R^1 and R^2 is a group (IA):



(IA)

and the other R^1 or R^2 is selected from hydrogen, C_{1-4}alkyl, C_{1-4}alkoxy, carbocyclyl, heterocyclyl, carbocyclyloxy and heterocyclyloxy; wherein this R^1 or R^2 is optionally substituted on carbon by one or more groups selected from R^5; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen is optionally substituted by C_{1-4}alkyl;

Ring A is pyridin-2-yl or thiazol-2-yl; wherein said pyridin-2-yl or thiazol-2-yl is optionally substituted on carbon by one or more groups selected from R^6;

one of R^3 and R^4 is hydrogen and the other is selected from hydrogen, C_{1-4}alkyl, C_{1-4}alkoxy, carbocyclyl, heterocyclyl, carbocyclyloxy and heterocyclyloxy; wherein

R^3 and R^4 are independently optionally substituted on carbon by one or more groups selected from R^7; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen is optionally substituted by C_{1-4}alkyl;

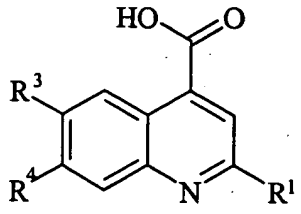
R^6 is selected from halo, carboxy and C_{1-4}alkyl;

R^5 and R^7 are independently selected from halo, C_{1-4}alkyl, C_{1-4}alkoxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, carbocyclyl, heterocyclyl, carbocyclyloxy, heterocyclyloxy and carbocyclylidenyl; wherein R^5 and R^7 is independently optionally substituted on carbon by one or more R^8; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen is optionally substituted by C_{1-4}alkyl; and

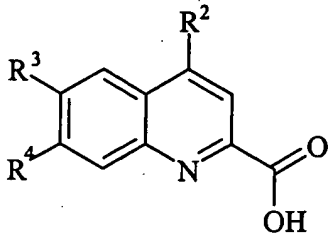
R^8 is selected from halo, carboxy, methyl, ethyl, methoxy, ethoxy, methylamino, ethylamino, dimethylamino, diethylamino and *N*-methyl-*N*-ethylamino,

or a salt, solvate or pro-drug thereof, which process ~~(wherein variable groups are, unless otherwise specified, as defined in Claim 1)~~ comprises:

Process 1): reacting an acid of formula **(IIa)** or **(IIb)**:

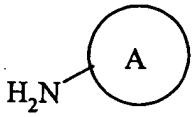


(IIa)



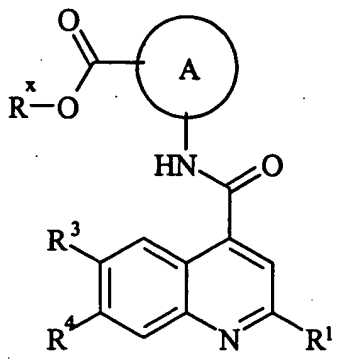
(IIb)

or an activated derivative thereof; with a compound of formula **(III)**

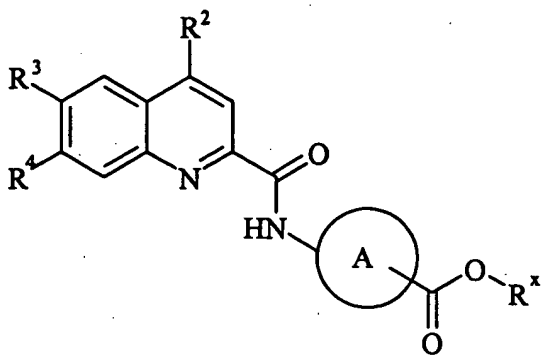


(III); or

Process 2) for compounds of formula **(I)** wherein R^6 is carboxy; deprotecting a compound of formula **(IIIa)** or **(IIIb)**:



(IIIa)



(IIIb)

wherein $R^xC(O)O$- is an ester group;

and optionally further comprises ~~thereafter if necessary or desirable~~:

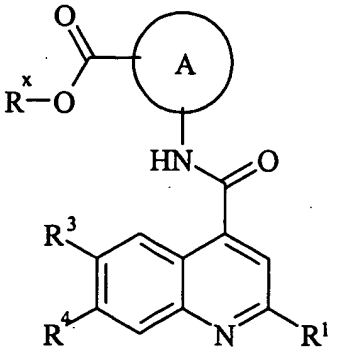
i) converting a compound of the formula (I) into another compound of the formula (I);

~~and/or~~

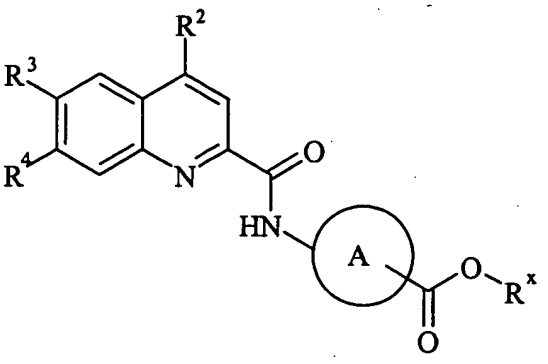
ii) removing any protecting groups; ~~and/or~~

iii) forming a salt, solvate or pro-drug thereof; or a combination thereof.

10. (Currently Amended) A compound of formula (IIIa) or a compound of formula (IIIb): ~~as defined in Claim 9~~



(IIIa)



(IIIb)

wherein:

$R^xC(O)O$- is an ester group;

R^1 or R^2 is selected from hydrogen, C_{1-4}alkyl, C_{1-4}alkoxy, carbocyclyl, heterocyclyl, carbocyclyloxy and heterocyclyloxy; wherein this R^1 or R^2 is optionally substituted

on carbon by one or more groups selected from R^5; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen is optionally substituted by C_{1-4}alkyl;

Ring A is pyridin-2-yl or thiazol-2-yl; wherein said pyridin-2-yl or thiazol-2-yl is optionally substituted on carbon by one or more groups selected from R^6;

one of R^3 and R^4 is hydrogen and the other is selected from hydrogen, C_{1-4}alkyl, C_{1-4}alkoxy, carbocyclyl, heterocyclyl, carbocyclyloxy and heterocyclyloxy; wherein R^3 and R^4 are independently optionally substituted on carbon by one or more groups selected from R^7; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen is optionally substituted by C_{1-4}alkyl;

R^6 is selected from halo, carboxy and C_{1-4}alkyl;

R^5 and R^7 are independently selected from halo, C_{1-4}alkyl, C_{1-4}alkoxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, carbocyclyl, heterocyclyl, carbocyclyloxy, heterocyclyloxy and carbocyclylidenyl; wherein R^5 and R^7 is independently optionally substituted on carbon by one or more R^8; and wherein if said heterocyclyl contains an -NH- moiety that nitrogen is optionally substituted by C_{1-4}alkyl; and

R^8 is selected from halo, carboxy, methyl, ethyl, methoxy, ethoxy, methylamino, ethylamino, dimethylamino, diethylamino and *N*-methyl-*N*-ethylamino.

REMARKS

Claims 1-10 are pending. Claims 1-3, 5 and 8-10 have been amended.

Claims 1 and 2 have been amended to recite "is optionally" or "are optionally" in lieu of "may be optionally".

Claim 3 has been amended to correct a typographical error.

Claim 5 has been amended to depend from claim 1.

Claim 8 has been rewritten as a method of treatment claim in order to encompass statutory subject matter.

Claims 9 and 10 have been rewritten as independent claims.

No new matter has been added.

Although Applicants believe no fees other than the filing fees are due, the Commissioner is hereby authorized to credit any overpayment or charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 18-1945, from which the undersigned is authorized to draw, under Order No. ASZD-P01-898. Please direct any questions arising from this submission to the undersigned at (617) 951-7633.

Dated: May 12, 2005

Respectfully submitted,

By _____

David P. Halstead, Ph.D.
Registration No.: 44,735
ROPES & GRAY LLP
One International Place
Boston, Massachusetts 02110-2624
(617) 951-7000
(617) 951-7050 (Fax)
Attorneys/Agents For Applicant